EFFECT OF BENZENE AND ITS HOMOLOGS ON UNIT ACTIVITY IN VARIOUS BRAIN STRUCTURES

L. I. Korytov

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KEY WORDS: unit activity; food motivation; benzene, toluene, xylene

Various external environmental factors are known to modulate the complex corticosubcortical mechanisms of motivations involved in the formation of behavioral acts [1, 4, 9]. The aim of the investigation described below was accordingly to study unit activity of single neurons of the sensomotor cortex (SMC), hippocampus (H), thalamus (T), and lateral hypothalamus (LH) in response to intravascular injection of benzene, toluene, and xylene and against the background of natural and artificially induced food motivation.

The chemical substances mentioned above are petrochemical products, widely used in various branches of the national economy, and by virtue of his activity, man may have contact with them either at work or during ordinary life. With respect to their physicochemical properties they are type II general anesthetics [3].

EXPERIMENTAL METHOD

Chronic experiments were carried out on 11 adult rabbits. To insert the microelectrode, with the aid of a micromanipulator, into the test brain structures, coordinates were taken from a stereotaxic atlas of the rabbit brain [7]. The position of the microelectrodes was verified histologically in sections through the layers of the brain by the "photoexpress" method.

Unit activity was recorded by glass microelectrodes filled with 3 M KCl solution. Unit activity was recorded on magnetic tape by a type 7003 measuring tape recorder ("Brüel and Kjaer," Denmark). Statistical and correlation methods of analysis of neuronal activity were carried out on an "Apple II" minicomputer (USA), using a program worked out in the Laboratory of General Physiology of Functional Systems, P. K. Anokhin Research Institute of Normal Physiology. Benzene, toluene, and xylene (20 mg/kg) were injected into the marginal vein in the course of 5 min. Natural food deprivation was produced in the animals by starvation for 24 h, artificial deprivation by subcutaneous injection of pentagastrin (20 mg/kg) into the previously fed animals. To block food motivation, the α-adrenoblocker phentolamine (10 mg/kg) was used. The animals were allowed water ad lib. Altogether 106 neurons were studied, including 20 in food-deprived rabbits receiving benzene (seven in SMC, eight in H and five in T), in animals receiving toluene 51 (17 in SMC, 17 in H, 17 in T), those receiving xylene 21 (T), and in previously fed animals, 14 neurons (nine in SMC and five in LH).

EXPERIMENTAL RESULTS

Analysis of the unit activity of the brain structures studied showed that 5-10 min after intravenous injection of benzene, a shift of the dominant intervals characteristic of hungry animals was observed, with the appearance of an additional dominant interval in the region of <1000 msec, and was recorded throughout the experiment (35-40 min), and only in two cases (25%) was this dominant interval absent in the hippocampal region after 35 and 40 min. The appearance of the interval in the region of 1000 msec or more indicates infrequent spike activity (Fig. 1). The presence of a well-defined interspike interval in the 1000 msec range was more characteristic of SMC than of T. The difference is statistically significant ($p < 0.05$).

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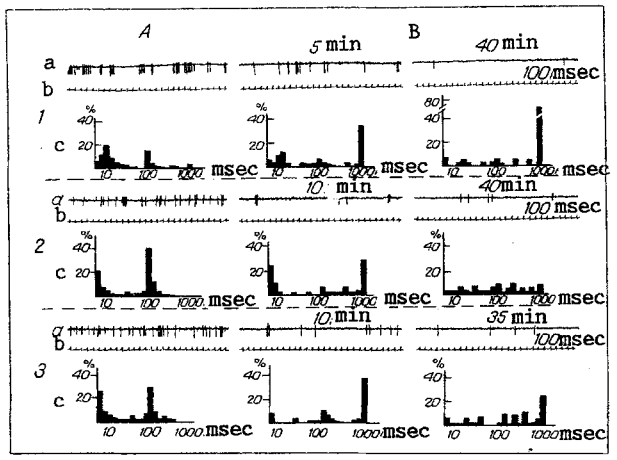

Fig. 1. Unit activity and interval histograms of pattern of SMC (1), H (2), and T (3) neurons of hungry rabbits before (A) and 5, 10, 35, and 40 min after (B) injection of benzene. a) Neuronal discharge, b) time marker 100 msec, c) interval histograms of unit activity (abscissa, interspike intervals, in msec; ordinate, frequency of detection of interspike intervals (in %).

After injection of toluene the same rule was observed but dominance of the interspike interval in the region of <1000 msec for SMC was observed in 88.2%, for H in 42.8%, and for T in 44.4% of cases. The appearance of this dominant interval on the histogram for SMC occurred at the 5th-10th minute, and for H and T at the 10th-15th minute.

The appearance of an interspike interval in the range of <1000 msec in the thalamic region in response to injection of xylene at the 10th-15th minute was observed in 28.6% of neurons tested.

A polymodal distribution of interspike intervals within different periods of the interval histogram (Fig. 1) occurred periodically in the structure of the spike train of the neurons in parts of the brain studied after injection of benzene and its homologs (Fig. 1).

As the experiments of this series showed, injection of benzene and its homologs caused both a decrease in the number of spikes, or even complete inhibition of the original unit activity, and also the periodic appearance of a polymodal distribution of the neuronal spike train on the interval histograms, possibly connected both with the absence of involvement of the particular cell in systemic processes connected with any kind of biological motivation, but on the other hand, this type of distribution is also characteristic of the initial stage of stress [2].

The question accordingly arose of the neurochemical mechanisms of this effect of benzene and its homologs on formation and realization of hunger motivation in animals.

We now know [5, 8, 10] that hunger motivation may be formed under the influence of mediators (noradrenalin etc.) and peptides (pentagastrin etc.), and is manifested in a specific form of activity of neurons in different brain structures, with dominance of two modes in the 1-20 and 100-200 msec range on the histogram of interspike intervals; the first peak, moreover, is more specific for this particular motivation.

To solve the above problem a series of experiments was carried out in which spike activity of SMC and LH neurons of fed animals was recorded after injection of benzene and against the background of the specific action of pentagastrin.

The initial spike discharge of the SMC and LH neurons of fed animals (Fig. 2) was characterized by a monomodal distribution of interspike intervals with mean values in the 100-2000 msec region. Subcutaneous injection of pentagastrin caused chewing in the animals after 4-5 min, and additional feeding thereafter caused a change in the structure of the spike train of the neurons, with dominance of two interspike intervals in the 1-20 and 100-200 msec region; these results confirm those obtained previously [6].

After injection of benzene against the background of artificially induced food motivation by pentagastrin (Fig. 3) a change in the spike train took place in SMC after 10-20 min, from a bimodal to a trimodal distribution of interspike intervals in the 1-20, 100-200, and 1000 msec range; the last mode, moreover, was observed in 77.7% of cases. Unit activity of LH was virtually unchanged, and only in two cases was there a change from one of the two dominant interspike intervals to the mode at 20-40 msec.

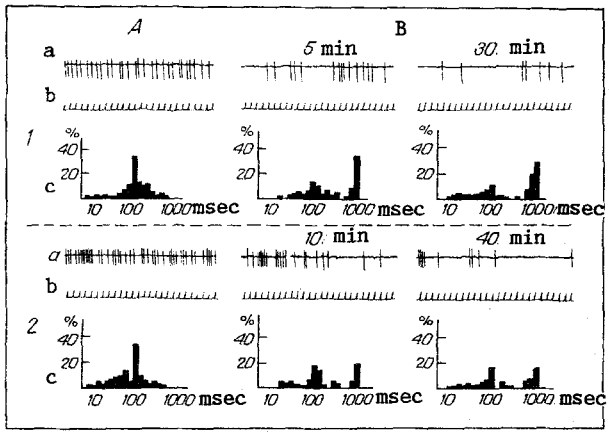

Fig. 2. Spike activity and interval histograms of pattern of SMC (1) and LH (2) neurons of fed rabbits before (A) and after injection of pentagastrin (B), benzene (c), and phentolamine (d) against the background of the action of (b) and (c). Legend as to Fig. 1.

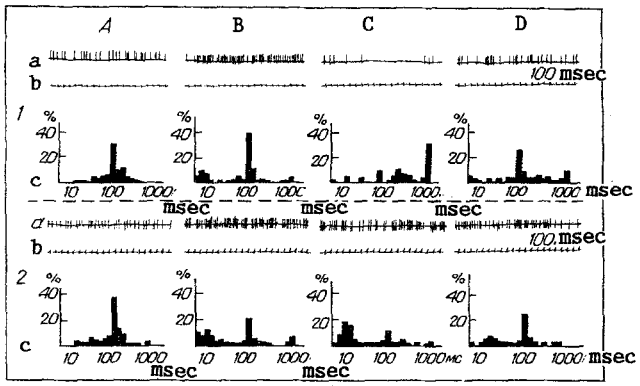

Fig. 3. Spike activity and interval histograms of pattern of SMC (1) and LH (2) neurons of fed rabbits before (A) and after injection of pentagastrin (B), benzene (C), and phentolamine (D) against the background of the action of (B) and (C). Legend as to Fig. 1.

Injection of phentolamine 45-50 min after artificially induced food motivation by pentagastrin and against the background of the action of benzene caused reorganization of the pattern of neuronal activity, with a change from the bimodal and trimodal distribution of interspike intervals to monomodal, characteristic of fed animals (Fig. 2).

The results of these experiments thus show that peptides and mediator processes, like the chemicals which were used (benzene and its homologs), can modulate spike trains of neurons taking part in the formation of food-getting behavior.

When the results of the effect of benzene and its homologs on neuronal activity are analyzed in different brain structures, it must be noted that the sequence and degree of intensity of the observed specific inhibitory effect differ in the discharge activity of the neurons of these structures. The experiments showed that in the evolutionary younger neocortex the inhibitory effect is quicker and stronger than in subcortical structures, and it is perfectly possible that this is one of the mechanisms responsible for animal behavior under the influence of benzene and its homologs, as chemical stressor agents.

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PRELIMINARY INJECTION OF PERFLUOROCARBON EMULSION – A NEW METHOD OF ANTIISCHEMIC PROTECTION OF THE MYOCARDIUM

S. I. Vorob'ev, Yu. V. Ladilov, V. V. Obraztsov, and G. R. Ivanitskii

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Preliminary pharmacological preparation of the donor, with the use of β-blockers, calcium antagonists, and antioxidants, is an effective method of protecting the myocardium against ischemic and reperfusion damage [1, 8].

The use of perfluoro compounds (PFCs), widely used because of their physicochemical properties in biology and medicine as gas-carrying [2] and biologically active [3, 13] media, in the context of the present investigation may prove to be promising.

As investigations conducted at the Institute of Biophysics, Academy of Sciences of the USSR, showed the mechanism of biological action is evidently linked with direct interaction between the PFC emulsion and its components and cell membranes [4-7, 9, 10, 12].

The aim of this investigation was to study the effect of preliminary administration of PFC emulsion on the myocardium.

EXPERIMENTAL METHOD

Experiments were carried out on rabbits weighing from 2 to 3 kg, divided into seven groups: group 1) receiving no injections (control, $n = 6$); animals of the other groups received preliminary injections as follows, 1, 12, and 24 h before ischemia: salt solution – group 2 (control injection, $n = 15$) and a 4% solution of Proxanol 268 in a salt composition – group 3 ($n = 11$) in doses of 20 ml/kg, and also an emulsion of PFC (perfluorane) with particle diameter of 0.1 μ, stabilized with 4% solution of Proxanol 268 (copolymer unit of polyethylene and polypropylene oxides, mol. wt. 7500, fraction of hydrophobic unit 0.2). The PFC phase in perfluorane was 10 vols. 2. Perfluorane was added in doses of 5 ($n = 11$), 10 ($n = 13$), 20 ($n = 16$), and 30 ($n = 16$) ml/kg – groups 4, 5, 6, and 7 respectively. The crystalloid composition of perfluorane and of the control solution was the same, and they consisted of the following ingredients (in mM): NaCl – 102, KCl – 5, $MgCl_2$ – 1.2, NaH_2PO_4 – 1.2 $NaHCO_3$ – 15, glucose 11. After preliminary injection of perfluorane or the control solutions (without oxygenation) into a rabbit 1, 12, and 24 h before ischemia, the heart was removed from the animal and perfused by Langendorff's method, spontaneously, on recirculation mode for 30 min with Krebs–Henseleit solution (KHS; initial level) under a constant perfusion pressure

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